

**Notice of Allowability****Application No.**

09/653,961

**Applicant(s)**

WU, GUANG-JER

**Examiner**

Stephen L. Rawlings, Ph.D.

**Art Unit**

1642

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--**

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 07 October, 2003.
2. ☒ The allowed claim(s) is/are 2,5,12,21 and 22.
3. ☐ The drawings filed on \_\_\_\_\_ are accepted by the Examiner.
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) ☐ All    b) ☐ Some\*    c) ☐ None    of the:
    1. ☐ Certified copies of the priority documents have been received.
    2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
    3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\* Certified copies not received: \_\_\_\_\_.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

**THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
  6. ☐ CORRECTED DRAWINGS ( as "replacement sheets") must be submitted.
    - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review ( PTO-948) attached
      - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date \_\_\_\_\_.
    - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date \_\_\_\_\_.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

**Attachment(s)**

1. ☒ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO-1449 or PTO/SB/08),  
Paper No./Mail Date 20031014
4. ☐ Examiner's Comment Regarding Requirement for Deposit  
of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☐ Interview Summary (PTO-413),  
Paper No./Mail Date \_\_\_\_\_.
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other \_\_\_\_\_.

### EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for entry of this examiner's amendment was given by Heeja Yoo-Warren on March 18, 2004.

The application has been amended as follows:

Amendments to the Claims:

1. (Canceled)
2. (Currently Amended) The method of claim 21 or 22, wherein said prostate cancer cell is from a biopsy tissue sample from a patient [for whom a prediction of metastasis of prostate cancer is sought].
- 3-4. (Canceled)
5. (Currently Amended) The method of claim 21 or 22, wherein the epitope of the MUC18 [antigen] polypeptide is [a] contained in the middle portion of the MUC18 polypeptide [and consists] consisting of [the] amino acid residues [of] 211-376 of the amino acid sequence as set forth in SEQ ID NO: 2.
- 6-11. (Canceled)
12. (Currently Amended) The method of claim 21 or 22, wherein said prostate cancer cell is a cell line cell.

13-19. (Canceled)

20. (Canceled)

21. (Currently Amended) A method of [predicting a risk for metastasis of] identifying a metastatic prostate cancer cell consisting essentially of measuring [the level of] expression of [a] the MUC18 coding sequence in [said] a prostate cancer cell, wherein the [level of] expression of the MUC18 coding sequence is determined by immunoassay using antibodies specific for an epitope of the MUC18 polypeptide consisting of the amino acid sequence set forth in SEQ ID NO: 2, whereby [the] a greater expression of the MUC18 coding sequence in said prostate cancer cell compared to that in a normal prostate cell indicates [a risk of metastasis for] the prostate cancer cell is metastatic.

22. (Newly Added) A method of identifying a malignant prostate cancer cell consisting essentially of measuring expression of the MUC18 coding sequence in a prostate cancer cell, wherein the expression of the MUC18 coding sequence is determined by immunoassay using antibodies specific for an epitope of the MUC18 polypeptide consisting of the amino acid sequence set forth in SEQ ID NO: 2, whereby a greater expression of the MUC18 coding sequence in said prostate cancer cell compared to that in a normal prostate cell indicates the prostate cancer cell is malignant.

Amendments to the Specification:

At page 7, line 11, “<sup>TM</sup>” has been inserted following “GenBank”.

At page 11, line 3, “<sup>TM</sup>” has been inserted following “GenBank”.

The following is an examiner's statement of reasons for allowance:

In the Amendment and Response filed October 7, 2003, Applicant has traversed the rejection of claims 2 and 21 under 35 USC § 102(b) as being anticipated by Liu et al. for the reasons set forth in section 5 of the Office action mailed April 8, 2003. Applicant has argued the claimed invention is not anticipated by the prior art because the antibodies of the claims are directed against peptide epitopes of the MUC18 polypeptide, whereas the antibody of the prior art was prepared against a carbohydrate antigen, not a peptide antigen. This argument has not been found persuasive, since to the contrary the claims do not require the antibody to bind a non-carbohydrate epitope of MUC18 polypeptide; nor claims to do the claims exclude an antibody prepared against a carbohydrate antigen. Rather, the claims are drawn to a method comprising measuring the level of expression of the MUC18 coding sequence by an immunoassay using "antibodies specific for an epitope of MUC18 polypeptide"; the epitope to which the antibody of the prior art binds is an epitope of the MUC18 polypeptide. Applicant has further argued the prior art does not anticipate the claimed invention because the antibody of the prior art binds a carbohydrate moiety, which is not found exclusively on the MUC18 polypeptide, but on cell surface proteins of many cell types. This argument has not been found persuasive since the claims do not exclude an antibody that binds non-exclusively to an epitope of the MUC18 polypeptide, or which also binds other proteins sharing the epitope recognized by the antibody. Nevertheless, Liu et al. teaches a higher expression of the antigen to which the antibody binds by prostate cancer cells is associated with a higher survival rate and a longer interval free of progression; whereas the claims recite a greater expression of the antigen in prostate cancer cells is indicative that the cells are malignant and/or metastatic, and the presence of malignant and/or metastatic cells is not associated with a higher survival rate and a longer interval free of progression. Accordingly, the rejection of claims 2 and 21 under 35 USC § 102(b) as being anticipated by Liu et al. for the reasons set forth in section 5 of the Office action mailed April 8, 2003 has been withdrawn.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue

fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

The literature cited in the attached In Form PTO-892 is pertinent to Applicant's disclosure. Wu et al. teaches correlation of MUC18 over-expression in prostate cancer cell lines and tissues with malignant progression.

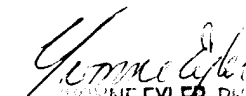
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne (Bonnie) Eyler, Ph.D. can be reached on (571) 272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Stephen L. Rawlings, Ph.D.  
Examiner  
Art Unit 1642

slr  
March 18, 2004

  
YVONNE EYLER, PH.D.  
LABORATORY PATENT  
TECHNOLOGY CENTER

### EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for entry of this examiner's amendment was given by Heeja Yoo-Warren on March 18, 2004.

The application has been amended as follows:

Amendments to the Claims:

1. (Canceled)

<sup>3</sup> ~~2~~. (Currently Amended) The method of claim <sup>1</sup> ~~21~~ or <sup>2</sup> ~~22~~, wherein said prostate cancer cell is from a biopsy tissue sample from a patient [for whom a prediction of metastasis of prostate cancer is sought].

3-4. (Canceled)

<sup>4</sup> ~~5~~. (Currently Amended) The method of claim <sup>1</sup> ~~21~~ or <sup>2</sup> ~~22~~, wherein the epitope of the MUC18 [antigen] polypeptide is [a] contained in the middle portion of the MUC18 polypeptide [and consists] consisting of [the] amino acid residues [of] 211-376 of the amino acid sequence as set forth in SEQ ID NO: 2.

6-11. (Canceled)

<sup>5</sup> ~~12~~. (Currently Amended) The method of claim <sup>1</sup> ~~21~~ or <sup>2</sup> ~~22~~, wherein said prostate cancer cell is a cell line cell.

13-19. (Canceled)

20. (Canceled)

<sup>1</sup>21. (Currently Amended) A method of [predicting a risk for metastasis of] identifying a metastatic prostate cancer cell consisting essentially of measuring [the level of] expression of [a] the MUC18 coding sequence in [said] a prostate cancer cell, wherein the [level of] expression of the MUC18 coding sequence is determined by immunoassay using antibodies specific for an epitope of the MUC18 polypeptide consisting of the amino acid sequence set forth in SEQ ID NO: 2, whereby [the] a greater expression of the MUC18 coding sequence in said prostate cancer cell compared to that in a normal prostate cell indicates [a risk of metastasis for] the prostate cancer cell is metastatic.

<sup>2</sup>22. (Newly Added) A method of identifying a malignant prostate cancer cell consisting essentially of measuring expression of the MUC18 coding sequence in a prostate cancer cell, wherein the expression of the MUC18 coding sequence is determined by immunoassay using antibodies specific for an epitope of the MUC18 polypeptide consisting of the amino acid sequence set forth in SEQ ID NO: 2, whereby a greater expression of the MUC18 coding sequence in said prostate cancer cell compared to that in a normal prostate cell indicates the prostate cancer cell is malignant.

Amendments to the Specification:

At page 7, line 11, “™” has been inserted following “GenBank”.

At page 11, line 3, “™” has been inserted following “GenBank”.